

Invasive Ductal Breast Carcinoma Underneath a Lipoma in a Male Patient

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ABSTRACT

Male breast cancer is a rare malignancy and accounts for less than one percent of all cancers in men. The authors describe the case of a 76-year-old Caucasian man with invasive ductal breast carcinoma who presented with a common lipoma. This paper reviews the current literature on epidemiology, risk factors, etiology, different types of breast cancer, clinical presentation, imaging, diagnostic workup, and treatment. (*J Clin Aesthet Dermatol.* 2012;5(10):33–37.)

A 76-year-old Caucasian man presented to the authors' clinic for evaluation of a painless lump on his left breast that had been present for six years, but recently grew over the last six months. The patient's past medical history was significant for basal cell carcinoma, hypertension, and hypercholesterolemia, controlled with atenolol, lovastatin, and hydrochlorothiazide. The patient reported no allergies. He denied smoking, but admitted to alcohol use. Review of systems was unremarkable. Patient denied nipple retraction, discharge, or ulceration. Physical examination revealed a well-developed, well-nourished male. Upon complete skin examination, the left lower quadrant of his left breast revealed a soft, rubbery, mobile, well-circumscribed mass about 2.5x2cm in diameter. An excisional biopsy of this mass was performed, which was consistent with a lipoma. However, upon further inspection and palpation of the area, a firm mass was felt in deeper tissue. The irregular mass was about 1.2x0.8cm in diameter, very firm, and noted to have a gray color. This mass was also sent for histological examination and revealed a 0.7cm, grade II invasive ductal carcinoma with microcalcifications. The patient did not exhibit any axillary lymphadenopathy and did not have any breast discharge. There were no abnormalities or masses noted in the contralateral chest wall or contralateral axilla. Following review of the histopathology, the patient was diagnosed with breast ductal carcinoma. A computed tomography (CT) was completed of his chest and abdomen, which demonstrated no metastasis. Since his initial visit, there has been no evidence of recurrence based on mammography taken six months post-biopsy. The patient was referred to surgery for

excision and oncology for further workup, including genetic testing, hormonal testing on the pathological tissue, and possibly adjunctive chemotherapy or radiation. The patient is currently under strict surveillance with regular complete cutaneous exams and mammography every six months with oncology. This case report serves to raise awareness of any growths presenting in the breasts of both male and female to exclude breast carcinoma as an underlying pathology. The authors examine the current literature surrounding male breast carcinoma.

DISCUSSION

Epidemiology. Currently, male breast carcinoma accounts for less than one percent of all cancers in men and is only 0.7 percent of all breast cancers.^{1,2} Male breast cancer leads to less than 0.1 percent of cancer-related deaths in men.³ The male-to-female ratio for breast cancer is 1:100.⁴ The peak incidence at which breast cancer affects men is age 71⁵ and usually develops after the age of 60.⁶ The median age of diagnosis in men is 65 years old.⁷ Men are diagnosed with breast cancer later than women⁵ by 5 to 10 years.⁸ There have been cases of breast cancer occurring in males between the ages of 13 and 32.^{1,5,9,10} Miao et al's data show that male breast cancer has remained stable over the last 38 years internationally.¹¹ The current literature states that the incidence of breast cancer in men is 1 case in every 100,000 men.⁵ In 2010, 1,970 breast cancer cases were diagnosed in men in the United States, with 390 predicted to end in death.¹² In 2009, the United States had 1,900 new diagnosed cases of male breast cancer and 440 deaths.¹³ Ashkenazi Jews¹⁴ and African American men have a higher prevalence

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compared to Caucasian men.¹⁵

Risk factors/etiology. The greatest risk factor for male breast cancer is Klinefelter's syndrome, which increases male breast cancer risk by 50-fold.^{10,16} Klinefelter patients have a lifetime risk of male breast cancer of five percent.¹⁷ A family history of breast cancer in men has an estimated odds ratio of 3.98 for developing breast cancer¹⁸ and a relative risk of 2.5.¹⁸ Genetic and hormonal imbalances play a major role in male breast cancer. BRCA2¹⁹ is a strong risk factor, although BRCA1 has also been reported.²⁰⁻²² Men who present with breast cancer should undergo genetic counseling and testing.²³ Currently, the National Comprehensive Cancer Network recommends that patients with BRCA1/2 mutations should be taught how to undergo breast self-examination.²³ Mutations in CHEK2 (1100delC) also increase the risk of male breast cancer by 10-fold²⁴ and genetic variants at chromosomes 2q35, 5p12, 6q25.1, 10q26.13, and 16q12²⁵ have been associated with male breast cancer. A possible etiology for male breast cancer is disease secondary to hormonal abnormalities,⁵ lack of androgen,²⁶ increased estrogen exposure,^{2,27,28} estrogen administration,²³ or estrogen-related disease including, but not limited to, gynecomastia,²⁹ cirrhosis,³⁰ and obesity. The increase in breast cancer in men has been attributed to a possible increased estrogen conversion in adipose tissue.²⁸ Also, testicular trauma,⁵ congenital inguinal hernia,³¹ orchitis, orchidectomy,³¹ Cowden's disease,³² radiation,⁵ and family history of breast or ovarian cancer¹⁷ predispose to the pathology. An increased risk of breast cancer has also been noted in patients who have a history of occupational exposure to blast furnaces, rolling mills, motor vehicle manufacturing, and steel works.³³ The patient described in this case did not have a history of previous occupational exposure. Other risk factors include low level of physical activity³⁴ and a history of bone fracture after age 45.³⁴

Types of breast cancer in men. Ninety percent of male breast carcinomas are of an invasive type with the most common being infiltrating ductal carcinoma, which accounts for more than 65 to 95 percent.^{8,35} Papillary carcinomas represents 2.6 percent³⁶ of cases and mucinous carcinomas 1.8 percent of cases.³⁶ Lobular carcinomas represent 1.5 percent of cases.⁸ Other subtypes, including medullary, mucinous, tubular, and squamous carcinomas have been reported in isolated case reports with less frequency in men compared to women. Paget's disease and inflammatory carcinoma present equally in males and females, but have rarely been reported in men.³⁷ Men tend to have a higher expression of hormone receptor, specifically 90 percent of male breast cancers express estrogen receptor positivity and 80 percent express progesterone receptor positivity.⁸ The degree of Her2-neu overexpression in men is less than women (2–15%).³⁸⁻⁴⁰

Clinical presentation. The most common presentation of a male with breast cancer is a painless palpable lump located subareolarly.^{1,4} Male patients also sometimes present with other symptoms, including nipple pain, bleeding, retraction, ulceration, or discharge.³² Lymphadenopathy may also be present.⁴¹ Gynecomastia is

present in 6 to 38 percent of cases of male breast cancer.⁴² Male breast cancer typically affects the right breast, which is similar to females.^{1,4} The possibility of a contralateral breast cancer developing in men is higher than women,⁴³ specifically 30-fold,⁴⁴ but the absolute risk is 0.1 percent per year.^{44,45} The differential diagnosis for male breast cancer includes breast abscess, lipoma, gynecomastia, metastases to the breast, and sarcomas.⁴³

Workup/imaging. Imaging that can be carried out include mammography, which can detect whether the lesion is malignant or benign.^{1,4} Because of the rarity of the disease, mammography is not needed for screening purposes.⁸ The National Comprehensive Cancer Network (NCCN) recommends screening for BRCA mutations in men who develop breast cancer, have a strong family history of breast cancers, or are from a family with a known BRCA mutation. The NCCN recommends that BRCA mutation carriers should have monthly breast self-examination and breast exams by a physician every 6 to 12 months starting at age 35 and baseline mammogram at age 40. The NCCN does not have any guidelines for breast cancer screening in men with other inherited high-risk conditions including Klinefelter,⁴⁶ although some literature advocates for a baseline mammography, followed by annual mammography and semiannual breast examination in Klinefelter patients.⁴⁷ Mammography has a sensitivity and specificity of 92 and 90 percent, respectively, in male breast cancer.⁴⁸ It can also be used to differentiate between malignancy and gynecomastia.⁴³ Microcalcifications are less common on mammography in male breast cancer when compared to female breast cancer.⁴³ Ultrasound can be used for nodal involvement.⁴⁷ Core biopsy is used for definitive diagnosis,^{32,48} which means that fine needle aspiration can also be used in males as it is very sensitive and specific. Once a lesion has been confirmed to be malignant, the tumor stage should be assessed and the tissue should also be evaluated for hormone receptor status. The tumor staging should follow the American Joint Committee on Cancer classification system, which includes tumor size, nodal involvement, and distant metastases.⁴⁹ Histological tumor grading should be assessed using the Scarff-Bloom-Richardson histological system. Immunohistochemical analysis should be done at this time to assess hormone receptor status of estrogen (ER) and progesterone receptor (PR). Metastases are examined the same way as in female breast cancer—through lab work, chest x-ray, bone scan, and CT scan of the abdomen and pelvis.⁴⁶ The literature does not have any recommendation for follow-up imaging after diagnosis. The authors' recommendations would be to follow the same guidelines for female breast cancer recommended by American Society of Clinical Oncology. Its recommendation consists of first post-treatment mammogram one year after the initial mammogram that leads to diagnosis, but no earlier than six months after definitive radiation therapy. Subsequent mammograms should be obtained every 6 to 12 months as indicated for surveillance of abnormalities. After consistent mammographic findings, mammography may be performed annually.⁵⁰

Treatment. Overall, the most effective treatment should be targeted toward the stage of the disease, the patient's overall health, the age of diagnosis, the presence of hormone receptor HER2, and BRCA.²³ Current treatment recommendations are not based on data from clinical studies in men, but the most agreed upon standard treatment in the literature is modified radical mastectomy with axillary lymph node dissection or sentinel lymph node biopsy (SLNB). Male patients who present with a solitary tumor with no metastasis should have a modified radical mastectomy with axillary lymph node dissection.^{2,51} Sentinel lymph node biopsy can be done in patients with a clinically negative axilla to avoid invasive axillary dissection.⁵² Males who have ductal carcinoma *in situ* (DCIS) should undergo lumpectomy followed by breast irradiation,²³ while smaller invasive tumors can be treated with lumpectomy and sentinel node biopsy followed by adjuvant radiation therapy.²³ For locally advanced tumors, loco regional radiation to chest wall and lymph nodes should be done.²³ Overall, sentinel node biopsy is one of the most effective ways of assessing nodal involvement.^{53–55} Due to the high prevalence of estrogen receptor positivity in male breast cancers, first-line standard adjuvant therapy is tamoxifen.⁵⁶ Tamoxifen has shown to improve survival and recurrence in male breast cancer associated with estrogen receptor positivity⁴⁸ and men who are treated with tamoxifen have better prognosis and survival rates.^{57–59} Goss et al⁵⁸ conducted a study of 57 patients who had significant improvement with tamoxifen. Tamoxifen has been effective in treating metastatic male breast cancer, which Cutili et al⁶⁰ demonstrated in their study of 243 node-positive men and saw cancer rates reduced from 62 to 28 percent.^{7,60} This is also consistent with other studies.^{61,62} Tamoxifen compliance in men has been challenging due to the drug not being tolerated.^{63,64} Five years of adjuvant tamoxifen is recommended for men with HR-positive breast cancer after mastectomy is performed.⁶⁵ There is conflicting information in terms of when radiation should be given. Male patients typically receive radiation more often than female patients, due to more advanced stage when diagnosed.^{32,47,66} Indication for radiation therapy comes from the data from female breast cancers, which includes large tumors, axillary node involvement, and an advanced tumor stage.⁶⁰ Some of the more recent literature is advocating for a modified radical or simple mastectomy in addition to radiation therapy. If a lumpectomy is performed, adjuvant radiation should also be included,²³ including chest wall radiation.¹⁰ However, if lymph node or pectoral muscle invasion is present, radiotherapy following mastectomy should be performed.⁴¹ There is also conflicting information in terms of how radiation affects male breast cancer. One study shows that postoperative radiation prevents recurrence, but has no effect on patient survival.⁶⁷ Adjuvant radiotherapy appears to be effective in preventing recurrences in male breast cancer, but differences in mortality have not been identified.^{57,68–71} Adjuvant radiotherapy is advised in men with positive lymph nodes or tumor >5cm or margins positive.⁵⁰ Some of the literature states that adjuvant chemotherapy should be

added when disease is advanced or there is axillary node involvement.²³ Some chemotherapy options used include cyclophosphamide, methotrexate, and fluorouracil (CMF); 5-fluorouracil, epirubicin, and cyclophosphamide (FEC); and epirubicin and cyclophosphamide (EC).⁷² Thus far, no current data exist on the use of trastuzumab in male breast cancer. Adjuvant chemotherapy is recommended in the younger patient population, patients with larger tumors, and patients who have axillary node involvement.²³ To date, only one prospective study of adjuvant chemotherapy has been published in patients with male breast cancer.⁷³ Chemotherapy has been shown in retrospective data to decrease recurrence and improve mortality,^{74–76} and it has been shown to increase both 5-year and 10-year survival rates.^{56,72} Men with intermediate- or high-risk breast cancer and hormone receptor-negative tumors⁴⁶ or patients who become refractory to hormone therapy should receive adjuvant chemotherapy. The best follow up is clinical assessment and self-breast examination since most male breast cancers present with a palpable mass.⁶¹

Prognosis. The prognosis for male breast cancer is similar to women, with lymph node involvement and tumor size being the most determinant prognostic factor.⁸ Similar to women, prognosis is determined by staging of the tumor, although in men it is typically detected later indirectly. Mortality increases by 50 percent with lymph node involvement.²³ If the tumor measures between 2 and 5cm, mortality increases by 40 percent.²³ Mortality is also increased if the patient is greater than 65 years old,²³ but male sex is a favorable prognostic factor.⁷¹ Bourhahfour et al's study of 127 cases of male breast cancer revealed metastases in 41 cases (32%), with the bone being the most common site for metastasis.⁷⁷ Currently, the 5-year survival rate for male breast cancer stands at 60 percent and the 10-year survival rate at 40 percent.⁴³ The 5-year survival rate based on stage is as follows: stage I=78 percent, stage II=67 percent, stage III=40 percent; and stage IV=19 percent.⁸ Of all ethnicities, African American men tend to have a worse prognosis.¹⁷ Unfortunately, later detection in men is also due to men not having changes in symptoms in breasts similar to how females typically do.²³ However, male patients with breast cancer have a lower risk of death from breast cancer when compared to females when adjusting for higher age at diagnosis, different standard of treatment, and more advanced stage at diagnosis.⁷¹ Nearly half of newly diagnosed breast cancers in men are diagnosed at stage III or IV,³² even though Bourhahfour et al showed that 82 percent of cases were diagnosed at stage II or III. This further adds to the reason why masses on the male breast are not aggressively sought after. Earlier diagnosis leads to stronger success with treatment,⁵ but men are typically diagnosed initially with gynecomastia, causing treatment to be delayed. The later detection is most likely due to better and more frequent screening in women, but also the lack of awareness of male breast cancer contributes to it being ignored in many cases or being mistaken with gynecomastia. Symptoms of male breast cancer typically present later when compared to women, which also causes men to have a later diagnosis and worse prognosis.²⁷

CONCLUSION

Currently, the literature is lacking in clinical randomized trials on male breast cancer patients in terms of the best treatment and management. Furthermore, the pathophysiology of male breast cancer is not clearly understood at present. Most of the current literature is based on retrospective data and pilot studies and not on randomized prospective studies. Much high quality additional research needs to be done to improve our understanding of this disease. Additionally, although a rare disease, it is imperative that physicians examining any type of breast mass or swelling in a male patient should include breast carcinoma in their differential diagnosis.

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